TABLE I. Refractory AD is associated with elevated serum IgE

	N	Average age (y)	Female/male ratio	Median IgE (IU/mL)
Severe refractory AD	38	39	2.3:1	3922*
Moderate AD	23	35	2.4:1	358
Quiescent AD	12	34	1.4:1	44

*$P < .0001$ compared with quiescent AD and $P = .005$ compared with moderate AD.

TABLE II. Skin prick testing sensitivity to allergens

	Dust mite	Animal dander	Molds	Grass	Weeds	Trees	Foods
Severe refractory AD	30/36	30/36	27/35	26/35	23/35	22/35	23/35
Moderate AD	9/20	16/20	7/20	12/20	11/20	12/20	4/17
P value	.005	.73	.004	.36	.57	1.0	.007

environment and diets. The severe AD group may have had increased exposure to dust mites and molds in comparison with the moderate AD group because they lived in climates more conducive to the presence of these allergens in the environment. In addition to exposure, skin barrier defects that are found in AD may lead to this increased allergen sensitization.[2] Recent studies have found that loss-of-function mutations in the gene for filaggrin, a protein involved in skin barrier function, are associated with severe AD, as well as increased allergen sensitivity, elevated total IgE, and asthma.[3-5] Furthermore, it has been observed that asthma and allergic rhinitis are associated with filaggrin mutations only in the presence of AD.[6] These studies suggest that skin barrier dysfunction in AD could lead to allergen absorption through the skin and increased allergen sensitization. Alternatively, another recent article suggests that T_H2 immune responses may also contribute to acquired defects in the skin barrier. The authors hypothesize that chronic allergen exposure could contribute to reduced filaggrin expression in AD.[7] A prospective controlled clinical trial is needed to determine whether effective food elimination diets or indoor avoidance of dust mite and molds will enhance management of refractory AD.

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Supported by National Institutes of Health grant AR41256, General Clinical Research Center grant MO1 RR00051 from the Division of Research Resources, the Edelstein Family Chair in Pediatric Allergy and Immunology, and the University of Colorado Cancer Center.

Disclosure of potential conflict of interest: B. H. Salt owns stock in Novartis, Qiagen, and Roche. The other authors have declared that they have no conflict of interest.

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Available online December 30, 2006.
doi:10.1016/j.jaci.2006.11.006

Predictive values for skin prick test and atopy patch test for eosinophilic esophagitis

To the Editors:

Eosinophilic esophagitis (EE) is an increasingly reported disorder in the United States and Australia.[1,2] The Children's Hospital of Philadelphia has reported a 35-fold increase from 2 cases in 1994 to 72 cases reported in 2003.[3] The symptoms of EE are similar to symptoms of gastroesophageal reflux but do not respond to gastroesophageal reflux medications. Other symptoms of EE include dysphagia in older children and failure to thrive in infants.[3] Because of these diverse symptoms, EE can be diagnosed only by esophageal biopsy after aggressive treatment with gastroesophageal reflux medications with the finding of $\geq$20 eosinophils per high-power field (hpf).[3]

Foods have been shown to be the cause of EE through the use of elimination diets or elemental formulas.[4,5] Elemental diets have demonstrated resolution of symptoms and normalization of biopsies in greater than 95% of the patients.[3] Because of the poor palatability of elemental formulas, elimination diets based on skin prick tests (SPTs) and atopy patch tests (APTs)[4,5] or removal of the most common food allergens[6] have been tried with a similar rates (75%) of improvement. However, removal of the most common food allergens did not reduce eosinophils to a normal range (13.6 eosinophils/HPF),[6] whereas elimination diets when effective based on SPT and APT testing reduce counts to 1.1 eosinophils/HPF,[4,5] and elemental diets[3] reduced eosinophil counts to a normal range of 0 eosinophils/HPF.

One of the main criticisms of our method is that we eliminate a group of foods with resolutions of symptoms

TABLE I. Predictive values for SPT and APT*

	SPT				APT			
Food	**PPV**	**NPV**	**Specificity**	**Sensitivity**	**PPV**	**NPV**	**Specificity**	**Sensitivity**
Milk (n = 46)	95.7%	57.7%	42.3%	97.6%	83.3%	58.7%	43.5%	90.2%
Egg (n = 39)	84.8%	75.4%	65.1%	90.2%	78.3%	82.8%	62.1%	91.4%
Soy (n = 28)	70.0%	68.9%	37.8%	89.5%	66.7%	87.3%	66.7%	87.3%
Wheat (n = 26)	77.8%	64.7%	18.9%	96.5%	74.2%	83.9%	71.9%	85.5%
Corn (n = 26)	57.1%	71.3%	13.8%	95.4%	65.8%	93.9%	89.3%	78.0%
Beef (n = 23)	81.8%	74.7%	30.0%	96.9%	94.4%	87.0%	65.4%	98.4%
Chicken (n = 15)	50.0%	83.3%	26.3%	93.3%	66.7%	95.7%	80.0%	91.7%
Rice (n = 14)	50.0%	85.6%	13.3%	97.5%	59.1%	96.9%	86.7%	87.5%
Potato (n = 11)	60.0%	89.9%	25.0%	97.6%	53.8%	94.6%	63.6%	92.1%
Peanut (n = 10)	77.8%	97.6%	77.8%	97.6%	75.0%	97.6%	60.0%	98.8%
Oat (n = 9)	33.3%	90.1%	10.0%	97.6%	47.4%	98.5%	90.0%	87.0%
Barley (n = 9)	42.9%	90.8%	27.3%	95.2%	90.0%	98.7%	90.0%	98.7%

*n, number of patients with positive change in biopsy after diet modification.

and normalization of biopsies, but we cannot tell which foods are responsible for this improvement. Therefore, we examined a subgroup of patients in whom we could definitively identify the foods that were causing the disease and calculated the negative predictive values (NPVs), positive predictive values (PPVs), specificity, and sensitivity for SPT and APT. All patients in this cohort had EE on the basis of ≥20 eosinophils per HPF after at least 1 month treatment with a proton pump inhibitor. The group used for statistical evaluation were patients for whom we could identify the individual foods that caused EE on the basis of the following:

- Removal of an individual food led to normal esophageal biopsy (0 eosinophils/HPF), and/or
- Addition of an individual food led to increased esophageal eosinophils (greater than 20 eosinophils/HPF) on biopsy after a previously normal biopsy

This subgroup is similar to our entire EE cohort of 316 patients who have undergone APT and SPT. However, these patients had biopsies 1 to 2 months after single food introduction or removal of an individual food. These patients elected to have biopsies after individual foods for 2 reasons: (1) they wanted to definitive know the causative food, or they had only 1 to 3 positive foods on testing and were adding back a single food at a time (25 patients, 1 food; 27 patients, 2 foods; 22 patients, 3 foods). Therefore, we did not use the entire cohort for calculating the predictive values because patients improved when a collection of foods (3-5) was removed in the entire cohort, making it impossible to determine which food or foods were responsible for the improvement in biopsies or symptoms. The most common foods for APT in the entire cohort and the subcohort were the same: milk, wheat, corn, beef, egg, potato, chicken, soy, barley, oat, and rice.

The population was also similar to a previously described population in which there was a predominance of males (64 males, 30 females) and atopy (78% diagnosed with asthma, allergic rhinitis, or atopic dermatitis). Eighteen patients had atopic dermatitis, with 1 having severe atopic dermatitis. The average age was 6.4 ± 4.2 (range, 2-18) years, and 84% were white. SPT and APT were performed as previously described.[4]

The PPVs and NPVs along with specificity and sensitivity were calculated on the basis of identification of single foods causing increased eosinophils in biopsies. The values are listed for the 12 most common foods in Tables I and II. Milk and egg were the most common foods causing EE in 46 and 39 patients, respectively. The PPV for SPT was greater than 75% for milk, egg, beef, and peanut. This is better than traditional skin testing for IgE-mediated reactions, with PPV reported around 50%.[7] The predictive value for APT ranged from 94% for beef to 54% for potato. The specificity for APT ranged from 43% to 89%, lower than the reported 91% for APT in atopic dermatitis (AD).[8] The predictive values for the 5 most common foods for the subgroup in patients with AD are reported in Table III. The PPVs are better in the EE subgroup compared with the EE subgroup with AD, suggesting that the AD population had a lower sensitivity rate. Similarly, the sensitivity was better for EE (78% to 99%) than the published rate for atopic dermatitis (30% to 33%) with APT.[7]

Because EE is most likely a mixed IgE and non-IgE food-mediated reaction, the combination of SPT and APT in the management of EE has been effective and needs to be examined. The combination of the 2 testing methods had an excellent NPV (88% to 100%) for all foods except milk, which was very low at 41% (Table II). The PPV was greater than 74% for the most common foods (milk, egg, and soy), but dropped off as the food became a less common cause of EE. Similarly, the sensitivity for identification of foods causing EE ranged from 77% to 97%, depending on the food.

Therefore, the combination of SPT and APT in designing a diet plan has a high success rate for food elimination or food reintroduction in EE with the exception of milk. Milk's NPV was unacceptably low, suggesting that a

TABLE II. Predictive values for the combination of SPT and APT

	Combined SPT and APT			
Food	**PPV**	**NPV**	**Specificity**	**Sensitivity**
Milk	92.0%	40.9%	63.9%	81.8%
Egg	84.8%	87.5%	86.7%	85.7%
Soy	73.7%	92.9%	87.5%	83.9%
Wheat	76.5%	90.0%	81.3%	87.1%
Corn	63.4%	92.5%	86.7%	76.6%
Beef	85.2%	92.5%	82.1%	93.9%
Chicken	62.5%	98.6%	93.8%	88.5%
Apple	57.1%	97.7%	66.7%	96.6%
Rice	60.9%	100.0%	100.0%	88.8%
Potato	61.1%	97.4%	84.6%	91.4%
Peanut	71.4%	100.0%	100.0%	95.2%
Oat	50.0%	100.0%	100.0%	89.4%
Barley	73.3%	100.0%	100.0%	95.2%

negative test to milk on SPT and APT does not rule out milk triggering EE. Our method of dry milk powder may lead to false-negatives; therefore, alternative methods should be explored such as using liquid milk for APT, as in other studies,[9] or larger Finn Chambers (Allerderm Laboratories, Inc., Petaluma, Calif).

Is it possible to extend the subgroup analysis to the entire cohort? The fact that the population of the subgroup had similar APT and SPT to the entire cohort on APT and SPT would suggest that the predictive values could be extrapolated to the entire group, but additional studies are needed to confirm this. A potential confounding variable for the predictive values is that we did not monitor for contamination with other food. Also, similar to previous published results, the more positive APT had a higher but not significantly higher correlation with PPV. Using the current PPV and sensitivity for all of the foods, the combination of SPT and APT would correctly identify a correct diet in about 70% of the population with resolution of the symptoms and biopsies, with the remaining 30% requiring an elemental diet for resolution of their symptoms and biopsies, similar to our previous published results.[4,5] Therefore, we would suggest elimination diets based on positive foods found on APT and SPT and milk elimination regardless of the testing results can prevent the need for an elemental diet in a majority of children with EE.

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TABLE III. Predictive values for patients with atopic dermatitis and EE

	SPT		APT	
Food	**PPV**	**NPV**	**PPV**	**NPV**
Milk (n = 14)	84.6%	66.7%	100.0%	55.6%
Egg (n = 10)	87.5%	72.7%	71.4%	88.9%
Soy (n = 10)	33.3%	38.5%	80.0%	100.0%
Wheat (n = 5)	0.0%	76.5%	42.9%	77.8%
Peanut (n = 5)	100.0%	87.5%	NA	87.5%
Beef (n = 5)	66.7%	81.3%	42.9%	100.0%
Corn (n = 4)	0.0%	61.1%	50.0%	75.0%

NA, Not applicable.

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Disclosure of potential conflict of interest: J. M. Spergel has received grant support from Nutricia. C. A. Liacouras has consulting arrangements with Ception, Ross, SHS, and Nutricia; has received grant support from Wyeth; is on the speakers' bureau for TAP and AstraZeneca; and serves once a year as an expert witness in litigation and receives compensation for it. The rest of the authors have declared that they have no conflict of interest.

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